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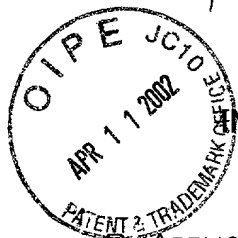
Date:

March 28, 2002

By:

Lynn Anderson

PATENT



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:

Peltine, *et al.*

EXAMINER: Unknown

SERIAL NO.: 09/810,919

ART UNIT: 1741

FILED: March 16, 2001

CONFIRMATION NO.: 7145

FOR: MICROLABORATORY DEVICES
AND METHODS

Preliminary Amendment

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, applicants respectfully request entry of the following amendments.

In the specification:

On page 18, please replace the paragraph starting on line 3 with the following:

Figs. 19A-C depict two adjacent tracks with a microparticle switching tracks.

On page 18, please replace the paragraph starting on line 20 with the following:

Fig. 26 depicts a top down view of a multi-chamber microlaboratory station used for reacting and incubating microparticles with a reagent that has multiple side ports interconnecting each chamber and utilizes side port access channels.

20110919-04110

On page 18, please delete the paragraph starting on line 22.

On page 18, please replace the paragraph starting on line 34 with the following:

Figs. 32A – D depict a micro-lab system having dynamic architecture.

On page 19, please replace the paragraph starting on line 7 with the following:

The problems discussed above, and other problems, are addressed by the present invention by providing apparatuses, methods, and devices for use in performing a desired laboratory and/or manufacturing activities in an automated, micro-scale format. Unlike the prior art, the invention utilizes, in preferred embodiments of one aspect, methods and devices using a substrate having a workplace defining x-y coordinates; one or more microparticles adapted for controlled movement adjacent the workplace where the microparticles are each adapted for having or inducible to have one or more magnetic or electrostatic dipoles. The dipoles may be physical dipoles such as a magnetic dipole made of permanent magnet material, or they may be apparent dipoles relative the background medium. For example, a non-magnetic sphere in a ferrofluid (a liquid with suspended colloidal magnetic particles) upon which a uniform magnetic field is imposed has an apparent dipole because the ferrofluid medium is magnetized and the non-magnetic sphere is not. The microparticles further include one or more laboratory effectors for performing a function. The microparticles navigate to and between one or more laboratory or manufacturing stations located at different known workplace x-y coordinates where each laboratory station is adapted to carry out or participate in one or more selected laboratory operations with the microparticle effectors. A driving structure, in some embodiments, is positioned adjacent the workplace where the driving structure has a plurality of drive elements selectively energizable to move one or more of the microparticles between selected workplace x-y coordinates, through interactions of the drive elements with the microparticles' dipoles; and, a controller operatively linked to the drive elements for energizing the drive elements to move the one or more selected microparticles between or among selected laboratory stations to accomplish the desired laboratory-activity.

On page 25, please replace the paragraph starting on line 23 with the following:

In some embodiments, the wells of the device are spatially arranged so that they are similar to commercially available plates such as microtiter plates (96 well, 384 well, etc.). In other embodiments, the device is configured to communicate with the spatial arrangement of a commercially available microtiterplate or similar well plate, so that materials may be either deposited to or acquired from such plates by the device.

On page 48, please replace the paragraph starting on line 27 with the following:

In Fig. 27F, panel 27F1, driving elements, not shown, are used to move microparticle 2791 such that open end of the capillary effector 2795 enters chemical reservoir 2793 to contact with a liquid contained therein. In Fig. 27F, panel 27F2, capillary effects pull an aliquot of the chemical into the capillary tube, but since the opposite end of the tube is closed, the entrapped gas pressure rises until it balances the capillary effects. Thus, the capillary tube pulls in a fixed amount of liquid chemical, but gas is entrapped at the closed end.

On page 48, please replace the paragraph starting on line 33 with the following:

Fig. 27F, panel 27F3 illustrates ejection or deposition of the chemical in the capillary. The micro particle has moved to another part of the system to deposit the chemical into a reaction chamber. Although in Fig. 27G, the reaction chamber is illustrated similar to the reservoir in Fig. 27F, other geometries can be used. In Fig. 27G, the liquid acquired by microparticle's 2791 capillary effector 2795 in Fig. 27F is urged or forced into from capillary effector 2795 into side port 2792, which is capillary side port, by heating gas previously entrapped within capillary effector 2795 when it was loaded with liquid and trapped at the closed end of the capillary effector, using an adjacent heat source (not shown in Fig. panel 27Ga). Other methods of heating the entrapped gas may be used, such as heating by laser, inductive heating, dielectric heating, conductive heating by contact with the microparticle, and others. As the gas is heated its pressure rises, forcing the chemical liquid out of the open end of the tube and into the reaction chamber. The temperature rise determines the expelling gas pressure. Typically, if the liquid chemical occupies a relatively small amount of the total tube volume, then each degree centigrade rise in temperature will raise the gas pressure by roughly 3000 dynes/cm² (300 Pa). This estimate can be made from the well known ideal gas law used to describe the pressure-volume-

temperature relation of most gases. The pressure rise needed to expel the liquid can be estimated by capillary formulas such as, $P_c = 2s / r$, where P_c is the capillary pressure from the liquid, r is the inner radius of the tube, and s is the surface tension of the liquid. For example, if the liquid has a surface tension of 50 dynes/cm, and the capillary has an inner radius of $r = 0.002$ cm (20 microns), then $P_c = 50000$ dynes/cm². The desired temperature rise of the gas is then estimated as roughly (50000/3000) C or about 17 degrees centigrade. The temperature rise can be reduced by increasing the tube radius if desired. It should also be noted that the temperature rise at the liquid end can be less than the average temperature rise of the gas if heating is concentrated at the opposite closed end. This consideration would be important, for example, using chemicals that are sensitive to temperature. In some embodiments, the microparticle with its capillary effector is eventually cycled back to repeat the process. In most configurations, each individual manipulator can spend only a portion of its time actively engaged in the deposition cycle, because the system's massive parallelism and high device speed allow high throughput, even without the use of all the manipulators for deposition at the same time. The manipulators' "free" time may, for example, be used for quality control tasks such as inspection, replacement, or testing the microparticles' deposition properties off line. In certain instances, excess reagent may be removed, for example to prevent the contamination of other deposition sites. A preferred process includes aspirating excess solution and washing individual spots repeatedly with wash solutions. This embodiment of a microparticle-levitating device is used for depositing liquid or solid quanta of chemical at selected locations on a substrate. In this system, the manipulators (effectors) are mobile, so material supply and handling is fully automated. The reagent reservoirs are simply placed in proximity to the system, and the manipulators pick up and deposit the chemicals as needed. The end effectors for chemical deposition are easy to inspect at one or a few inspection locations (e.g., using optical techniques), and their performance can even be tested off line with negligible effects on production, again because the manipulators are mobile.

REMARKS

Entry of the above amendments prior to examination is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims. The attached pages are captioned **"Version with Markings to Show Changes Made."**

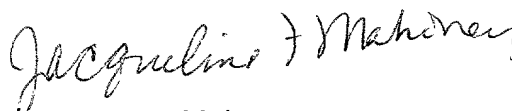
A. Amendments to the Specification

The specification has been amended to correct drawing numbering. The specification has further been amended to correct obvious typographical and grammatical errors.

The amendments to the specification add no new matter.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted,



Jacqueline F. Mahoney
Registration No. 48,390

Date: March 28, 2002

Correspondence Address:

Customer No. 22918
650 838-4300

201009.0410

Version with Markings to Show Changes Made

On page 18, please replace the paragraph starting on line 3 with the following:

Figs. 19A-C depict[s] two adjacent tracks with a microparticle switching tracks.

On page 18, please replace the paragraph starting on line 20 with the following:

Fig. 2[5]6 depicts a top down view of a multi-chamber microlaboratory station used for reacting and incubating microparticles with a reagent that has multiple side ports interconnecting each chamber and utilizes side port access channels.

On page 18, please delete the paragraph starting on line 22.

[Fig. 26 depict a top down view of a microlab system utilizing side port access channels.]

On page 18, please replace the paragraph starting on line 34 with the following:

Figs. 32A – [E]D depict a micro-lab system having dynamic architecture.

On page 19, please replace the paragraph starting on line 7 with the following:

The problems discussed above, and other problems, are addressed by the present invention by providing apparatuses, methods, and devices for use in performing a desired laboratory and/or manufacturing activities in an automated, micro-scale format. Unlike the prior art, the invention utilizes, in preferred embodiments of one aspect, methods and devices using a substrate having a workplace defining x-y coordinates; one or more microparticles adapted for controlled movement adjacent the workplace where the microparticles are each adapted for having or inducible to have one or more magnetic or electrostatic dipoles. The dipoles may be physical dipoles such as a magnetic dipole made of permanent magnet material, or they may be apparent dipoles relative to the background medium. For example, a non-magnetic sphere in a ferrofluid (a liquid with suspended colloidal magnetic particles) upon which a uniform magnetic field is imposed has an apparent dipole because the ferrofluid medium is magnetized and the non-magnetic sphere is not. The microparticles further include one or more laboratory effectors for performing a function. The microparticles navigate to and between one or more laboratory or manufacturing stations located at different known

workplace x-y coordinates where each laboratory station is adapted to carry out or participate in one or more selected laboratory operations with the microparticle effectors. A driving structure, in some embodiments, is positioned adjacent the workplace where the driving structure has a plurality of drive elements selectively energizable to move one or more of the microparticles between selected workplace x-y coordinates, through interactions of the drive elements with the microparticles' dipoles; and, a controller operatively linked to the drive elements for energizing the drive elements to move the one or more selected microparticles between or among selected laboratory stations to accomplish the desired laboratory-activity.

On page 25, please replace the paragraph starting on line 23 with the following:

In some embodiments, the wells of the device are spatially arranged so that they are similar to commercially available plates such as microtiter plates (96 well, 384 well, [etc.]etc.). In other embodiments, the device is configured to communicate with the spatial arrangement of a commercially available microtiterplate or similar well plate, so that materials may be either deposited to or acquired from such plates by the device.

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side port, by heating gas previously entrapped within capillary effector 2795 when it was loaded with liquid and trapped at the closed end of the capillary effector, using an adjacent heat source (not shown in Fig. panel 27Ga). Other methods of heating the entrapped gas may be used, such as heating by laser, inductive heating, dielectric heating, conductive heating by contact with the microparticle, and others. As the gas is heated its pressure rises, forcing the chemical liquid out of the open end of the tube and into the reaction chamber. The temperature rise determines the expelling gas pressure. Typically, if the liquid chemical occupies a relatively small amount of the total tube volume, then each degree centigrade rise in temperature will raise the gas pressure by roughly 3000 dynes/cm² (300 Pa). This estimate can be made from the well known ideal gas law used to describe the pressure-volume-temperature relation of most gases. The pressure rise needed to expel the liquid can be estimated by capillary formulas such as, $P_c = 2s / r$, where P_c is the capillary pressure from the liquid, r is the inner radius of the tube, and s is the surface tension of the liquid. For example, if the liquid has a surface tension of 50 dynes/cm, and the capillary has an inner radius of $r = 0.002$ cm (20 microns), then $P_c = 50000$ dynes/cm². The desired temperature rise of the gas is then estimated as roughly (50000/3000) C or about 17 degrees centigrade. The temperature rise can be reduced by increasing the tube radius if desired. It should also be noted that the temperature rise at the liquid end can be less than the average temperature rise of the gas if heating is concentrated at the opposite closed end. This consideration would be important, for example, using chemicals that are sensitive to temperature. In some embodiments, the microparticle with its capillary effector is eventually cycled back to repeat the process. In most configurations, each individual manipulator can spend only a portion of its time actively engaged in the deposition cycle, because the system's massive parallelism and high device speed allow high throughput, even without the use of all the manipulators for deposition at the same time. The manipulators' "free" time may, for example, be used for quality control tasks such as inspection, replacement, or testing the microparticles' deposition properties off line. In certain instances, excess reagent may be removed, for example to prevent the contamination of other deposition sites. A preferred process includes aspirating excess solution and washing individual spots repeatedly with wash solutions. This embodiment of a microparticle-levitating device is used for depositing liquid or solid quanta of chemical at selected locations on a substrate. In this system, the

manipulators (effectors) are mobile, so material supply and handling is fully automated. The reagent reservoirs are simply placed in proximity to the system, and the manipulators pick up and deposit the chemicals as needed. The end effectors for chemical deposition are easy to inspect at one or a few inspection locations (*e.g.*, using optical techniques), and their performance can even be tested off line with negligible effects on production, again because the manipulators are mobile.

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